



Docket No.: GLOF:007USC1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT

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In re Application of:
Gong et al.

Serial No.: 10/605,708

Filed: October 21, 2003

For: CHIMERIC GENE CONSTRUCTS FOR
GENERATION OF FLUORESCENT
TRANSGENIC ORNAMENTAL FISH

Group Art Unit: 1632

Examiner: Singh, Anoop Kumar

Atty. Dkt. No.: GLOF:007USC1

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CORRECTED APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Appellants hereby submit this Corrected Appeal Brief to the Board of Patent Appeals and Interferences pursuant to 37 C.F.R. §41.31(a)(1) and 41.37 in response to the Notification of Non-Compliant Appeal Brief mailed on July 29, 2009. The Status of the Claims section has been corrected and is attached herewith.

If any fees are due for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/GLOF:007USC1.

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I. REAL PARTY IN INTEREST

The real party in interest is the assignee, National University of Singapore. The subject matter of the application is currently licensed to Yorktown Technologies, L.P.

II. RELATED APPEALS, INTERFERENCES, AND JUDICIAL PROCEEDINGS

There are no related appeals, interferences or judicial proceedings that are related to, directly affect, or would be directly affected by, or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Claims 1-3, 9-15, 20-21, 24, 30-32, 35-44 and 45 are currently pending and under rejection; Appellants hereby appeal each rejection of all of these claims. Claims 4-8, 16-19, 22-23, 25-29, and 33-34 are canceled.

IV. STATUS OF AMENDMENTS

There are no pending amendments.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The main claim subject to rejection is claim 43, along with the support in the specification for each element (we note that the present application was electronically filed using early versions of the PTO electronic filing software, the printout of which had only page numbers and paragraph numbers), as follows:

43. A method of providing transgenic fish to the ornamental fish market [*page 8, paragraph 0013; page 39, paragraph 0091*], comprising the steps of:

(a) obtaining a transgenic fish line comprising one or more chimeric genes that are positioned under the control of a promoter that drives the expression of a fluorescent protein in muscles of said fish [*page 6, paragraphs 0009-0010; pages 13-14, paragraphs 0028-0029; pages 18-19, paragraphs 0040-0042*], said promoter being a muscle specific promoter [*Id.*], such that said transgenic fish expresses fluorescent protein encoded by the gene in skeletal muscle at a level sufficient such that said transgenic fish fluoresces upon exposure to one or more light [*pages 12-13, paragraphs 0022-0026; page 35-38, paragraphs 0080-0088*]; and

(b) distributing fish of said line to the ornamental fish market [*page 1, paragraph 0002; page 6, paragraph 0010; page 39-40, paragraphs 0091-0092*].

As can be seen, principal claim 43 does not require that the transgenic fish be capable of expressing at a high enough level to be visible in sunlight.

Turning to dependent claim 1, which depends from claim 43, it is noted that dependent claim 1 incorporates all of the limitations of claim 43, but further specifies that the selected transgenic line is capable of fluorescing upon exposure to sunlight [*see pages 37-38, paragraph 0085*].

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Whether claims 1-3, 9-15, 20-21, 24, 30-32, 35-44 and 45 are properly rejected under 35 U.S.C. §112, first paragraph (non-enablement);

B. Whether claims 1-3, 9-15, 20-21, 24, 30-32, 35-44 and 45 are properly rejected under 35 U.S.C. §112, first paragraph (lack of written description); and

C. Whether claims 1-3, 9-15, 20-21, 24, 30-32, 35-44 and 45 are properly rejected on the basis of obviousness-type double patenting of US 7,135,613.

VII. ARGUMENT

A. Whether claims 1-3, 9-15, 20-21, 24, 30-32, 35-44 and 45 are properly rejected under 35 U.S.C. §112, first paragraph (non-enablement)

The Final Rejection first rejects all of the pending claims on the basis of non-enablement. Of some importance is the fact that the Action concedes that essentially the same claim as claim 1, if limited to a particular promoter (zebrafish myosin light chain gene promoter), would be fully enabled. See Action at pages 2-3. Therefore, the only enablement issue is whether the specification, in view of the level of skill in the art at the time of filing, is enabling for the use of the well-known class of muscle specific promoters in general.

We would also note that the Final Action appears to treat the main claim, claim 43, as if it requires that the transgenic fish be capable of fluorescing in sunlight. This is not the case and no such requirement appears in the main claim – the main claim 43 simply states “at a level sufficient such that said transgenic fish fluoresces upon exposure to one or more light” – and the “light” can be, for example, blue light, fluorescent light, *etc.* Thus, Appellants remarks will initially address the rejections with respect to claim 43 and then turn to a consideration of dependent claim 1. Since claim 43 merely refers to selecting transgenic fish that expresses a fluorescent protein “at a level sufficient such that said transgenic fish fluoresces upon exposure to one or more light”, the issue for the Board with respect to claim 43 is merely whether the specification is enabling for the preparation of fish that have a detectable level of fluorescence when exposed to some kind of light.

Appellants would first note that the specification provides a complete description of two different muscle specific promoters that have been successfully employed in the practice of the claimed invention, including the muscle creatine kinase ("MCK") promoter and the myosin light chain ("MLC") promoter. Both of these muscle promoters were found to produce fluorescent transgenic fish ("fry") that express their fluorescence under light, in accordance with claim 43. See pages 35-38, paragraphs [0070] – [000088], particularly paragraphs [0082], [0084] and [0085], and Figs 8-12.

With respect to muscle promoters in general, which are admittedly well known in the art, Appellants refer to the Declaration of one of the inventors, Dr. Zhiyuan Gong (copy enclosed as Exhibit 1). Dr. Gong addressed a number of items in his Declaration relevant to the present appeal. For one, Dr. Gong addresses the question of the use of other muscle promoters to produce transgenic fish that express fluorescence that is visibly detectable, and explains generally why the generation of such transgenic fish, even when employing a relatively weak promoter, does not require an undue amount of experimentation. Moreover, Dr. Gong further provides evidence of the foregoing in the form of various scientific publications that have been successfully used subsequent to our priority date to achieve very high level expression of fluorescence genes in fish.

Dr. Gong starts off in paragraph 6 by noting that based on his knowledge and experience in the production of fluorescent, transgenic fish, essentially any muscle-specific promoter can be employed to produce very highly fluorescent founder embryos and lines. He continues by noting that while it may be necessary in some instances to use a screening procedure (such as the one spelled out in claim 43) to select those embryos that have appropriate position effects, this would

require only routine, repetitive steps. Dr. Gong further indicates that, of course, when a weaker promoter is employed it may be necessary to inject and screen larger numbers of embryos, which may be more than one thousand, to identify a “high expresser” but again such screening is straightforward and does not involve any additional inventiveness to accomplish. Dr. Gong concludes in paragraph 6 by stating that considering the muscle occupies a large part of the fish body and thus has the capacity to synthesize enough proteins for visible fluorescence, screening for visible fluorescence using any muscle-specific promoter provides specific guidance and predictable results for obtaining stable transgenic fish suitable for ornamental fish market.

Thus, Dr. Gong is testifying that the ability to obtain highly expressing fish is not ultimately *dependent* on the promoter. By using a highly expressing promoter, fewer embryos/fry will need to be screened as compared to using a poorer promoter, which may require that a much larger number of embryos/fry will have to be screened. However, as Dr. Gong points out, the screening method taught by his specification (and embraced by claim 43) is, in its practice, a routine procedure. See MPEP §2164; *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*, *Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) – all standing for the proposition that the fact that experimentation may be complex does not make it “undue” where such experimentation is, as here, routine.

In paragraph 7 of his declaration, Dr. Gong provides specific examples of others that have prepared fluorescent, transgenic fish in accordance with the claimed invention, first directing the reader to the attached article of Kinoshita entitled “Transgenic medaka with brilliant fluorescence in skeletal muscle under normal light” (*Fisheries Science*, 70:645-649,

2004; attached as exhibit to Gong declaration). Dr Gong notes that, as the title implies, this article describes the preparation of transgenic, fluorescent medaka having a brilliant fluorescence in skeletal muscle under normal light. According to Dr. Gong, in these studies the author employed the skeletal muscle actin promoter, and we would further note that this author employed a promoter and enhancer construct known by others in the art at about the same time as the filing of the present application (see page 645, col. 2, reference 17). The author concludes that “[o]range, as well as green and red fluorescence was discernable with the naked eye under both daylight and fluorescent light.” Page 646, col. 2 at bottom.

Dr. Gong then refers to page 648, col. 1, and observes that the author also mentions the article of Chou *et al.* (*Transgenic Res.*, 10: 303-315, 2001), which is said to teach fluorescent, transgenic medaka strains with the GFP gene under the control of the β -actin gene regulatory region, which fluorescence could be observed under natural lighting (see, e.g., Figure 6, page 312). We would further note that these authors also employed gene constructs that were known in the art prior to the filing of the present application (see page 304 – to top of page 305; section entitled “Plasmids”).

The foregoing observations set out in paragraph 7 of the Gong declaration are also of particular relevance to dependent claim 1, which specifies transgenic fluorescent fish that express a sunlight-visible fluorescence, in that both Chou and Kinoshita employ gene constructs that were known prior to Appellants filing date and using techniques similar to those outlined by the present inventors in the subject specification.

The Action is essentially devoid of any cognizable evidence that would support a *prima facie* conclusion of non-enablement of claim 43. The Action, at the top of page 5, refers to the

articles of Moss *et al.*, Higashijima *et al.*, Kuo *et al.*, Kim *et al.* and Hackett *et al.* (attached as Exhibits 2-6, respectively), and states that these references show “that in spite of these constructs being reproducibly expressed in a tissue specific manner, none of these promoters were suitable for use in generating transgenic ornamental fish because an unusually high level of expression is required in the muscle tissue to be of commercial value.” Thus, the Action concedes that the many and various muscle specific promoters are both reproducible and specific, the argument turns entirely on their “commercial value.” Such, of course, is a merely a matter of taste not an enablement issue – it is true that the licensee of the present invention, known commercially as “GloFish” (see www.glofish.com), has had much commercial success with its transgenic ornamental fish precisely because other potentially competing fish (imported from Asia) do not, in our estimation, exhibit a sunlight-visible fluorescence. Nonetheless, those fish are also being marketed commercially. Stated another way, what the Examiner is inappropriately relying on as evidence of “lack of commercial appeal” as evidence of “non-enablement.” Clearly, commercial acceptance or appeal is not relevant to enablement or operability. *Phillips Petroleum Co. v. U.S. Steel Corp.*, 673 F.Supp. 1278, 6 USPQ2d 1065, 1104-05 (D. Del. 1987), *aff’d*, 865 F.2d 1247, 9 USPQ2d 1461 (Fed. Cir. 1989) (commercial suitability not relevant to operability); *Ex parte Cole*, 223 USPQ 94, 95 (PTO Bd. App. 1983 (“We know of no statutory or case law requiring each and every compound within a claim to be equally useful for each and every contemplated application.”))

Moreover, while we would agree that *these* articles do not teach transgenic fish that express fluorescence under sunlight (claim 1), they certainly *do* teach fish that express

fluorescence under UV light, and have a fluorescence that would meet the limitations of claim 43.

Turning to the “evidence” of general non-enablement relied upon by the Examiner, the only scientific article that is commented upon is that of Gong *et al.*, which we will address below. The remaining articles, Moss *et al.*, Higashijima *et al.*, Kuo *et al.*, Kim *et al.* and Hackett, if anything, actually support enablement. For example, Moss *et al.* (Exhibit 2) would appear to *support* the enablement of claim 43 in that it discloses the use of a rat myosin light chain (MLC) promoter that successfully drives the detectable transient expression of green fluorescent protein in transgenic zebrafish embryos. The authors conclude that “[n]otably, the rat MLC transcription control regions present in our construct were capable of directing muscle-specific expression of the *gfp* in the zebrafish.” Page 97, col. 2. Similarly, Higashijima *et al.* (Exhibit 3) discloses the use of α -actin and β -actin muscle promoters to drive the detectable expression of fluorescence genes in zebrafish; Kuo *et al.* (Exhibit 4) relates to the use of a neuron-specific promoter from a mammalian nectin gene, which is shown to faithfully direct expression of heterologous reporter genes in zebrafish neuronal tissue; Likewise, Kim *et al.* (Exhibit 5) demonstrates neuron-specific expression of a chicken gicerin cDNA in transient transgenic zebrafish using a mouse neurofilament promoter (NFP). Lastly, the Hackett review article (Exhibit 6) simply reviews technology relating to transgenic zebrafish production, as it stood in 1993. Thus, if anything, the foregoing articles actually support enablement.

Turning to the Gong reference (Exhibit 7), this reference also stands for broad enablement of claim 43, and also dependent claim 1. Gong discloses many of the studies that underlie the examples of the present application, but extends these studies to additional

fluorescence genes. Gong goes on to note that green fluorescent protein expressing transgenic zebrafish have been produced using many different tissue specific promoters, and cites to 8 different references in the reference section for this proposition. See page 62, col. 2, at top. Each of these references appears to describe transgenic zebrafish that express fluorescence detectable, for example, using a fluorescent light.

While it is agreed that Gong stands for the proposition that truly exceptionally high expression can be achieved, in part, by using a strong muscle promoter, we would direct the Board's attention to the statements regarding this publication from paragraph 8 of Dr. Gong's declaration: "As can be seen from reading the excerpt [at page 62, col.2] referred to by the examiner, it merely stands for the proposition that 'one' consideration is the strength of the promoter, and that another consideration is the tissue specificity, with muscle promoters in general being preferred for this reason. However, nowhere does the article in any way state or imply that the MLC2 promoter is "vital" to producing our fluorescent transgenic fish. As explained above, we know that this particular promoter is not 'vital' in this regard."

Lastly, turning to dependent claim 1, Appellants find no *prima facie* basis for maintaining such a rejection. As conceded by the Examiner, we have set forth two working examples in the specification of transgenic fish that express a fluorescence gene at a high enough level to be seen in sunlight. While there are indeed examples of transgenic fish in the prior art that do not meet the limitations of the fish recited in claim 1 (Higashijima *et al.* being an example), there are also many examples of others who have, subsequent to our priority date, reported that sun-visible expression had been achieved (Kinoshita and Chou *et al.* being examples). Moreover, Dr. Gong has provided a detailed explanation as to how the specification enables, without undue

experimentation, the production of transgenic fish that could be used in the practice of claim 1. Moreover, the Examiner has not raised any evidence to rebut the testimony of Dr. Gong in this regard.

Applicants would note that in the paragraph bridging pages 9 and 10, the Action raises the issue of mating species of fish of one species to fish of another species. Presumably this recitation goes to enablement of claim 36-40, which include a step of mating of fish. It was not Appellants intention to claim a novel form of breeding. Thus, it is submitted that such claim will certainly be interpreted as covering only breeding of fish species that can conventionally be bred. Similarly, Appellants note a concern at the top of page 9 regarding multiple colors of fish. However, this rejection is simply not understood. Appellants will attempt to address this rejection in their Reply Brief if the Examiner would be so kind as to clarify. In any event, Appellants would note that the Gong publication describes fish obtained using combinations of color genes, using the methodology of the present invention.

Accordingly, in view of the foregoing, the Board is requested to overturn the Examiner's enablement rejection of the claims.

B. Whether claims 1-3, 9-15, 20-21, 24, 30-32, 35-44 and 45 are properly rejected under 35 U.S.C. §112, first paragraph (lack of written description)

Next, all of the pending claims are rejected under 35 U.S.C. §112, first paragraph, on the basis of written description. Appellants have reviewed and considered this rejection but fail to understand its basis, or how it is different from the enablement rejection addressed above, in that the Examiner's comments appear to be consistent with the enablement issue, not written

description ("This analysis is based on whether specification teaches essential or critical elements or which are not adequately described in the specification and which are not conventional in the art as of the applicants' effective filing date for genus of muscle specific promoter derived from any species that would be strong enough to display fluorescence under normal sunlight." Action at page 15).

To the extent that the Examiner is taking the position that the specification fails to disclose the genus of muscle specific promoters *per se*, we would note that the specification teaches the concept of using muscle specific promoters generically (see, *e.g.*, paragraphs [0009] – [0011]) and sets forth two specific, working examples of particular muscle specific promoters, the MCK and MLC promoters (see paragraphs [0019], [0021], [0023], [00025]-[0026], [0033]-[0034] and [0079]-[0090]). Moreover, the fact that numerous muscle specific promoters were well known in the art at the time of filing has not been questioned by the Examiner. See Action at page 15. Rather, the Examiner's position appears to be that the specification fails to identify all such muscle promoters that would particularly useful for expressing at a sufficient level to produce sunlight-visible fluorescence. *Id.*

In response, Applicants would first again note that the principal claim, claim 43, does not require that the transgenic fish produce sunlight-visible fluorescence. Thus, there does not appear to be any issue with respect to claim 43.

Dependent claim 1 does specify sunlight-visible expression. However, as explained by Dr. Gong in his declaration, there is no requirement *per se* for any *special* muscle specific promoter in order to practice the subject matter of claim 1. Dr. Gong testifies that it would be expected that *any* muscle specific promoter can be successfully employed for this purpose. See

paragraph 6, particularly in light of paragraphs 4-5 and 7. Thus, since the specification generically refers to muscle promoters *per se*, and sets forth two specific, working examples of such muscle promoters, and in view of Dr. Gong's testimony that he contemplates that any muscle promoter can be employed in the practice of the invention.

In response, it is first noted that there is no legal basis under the written description requirement that an applicant set forth in the claims the specific structures being claimed where, as here, the *class* of compounds being claimed are known to the prior art. Instructive in this regard is the Federal Circuit's recent decision in *Capon v. Eshhar v. Dudas*, 418 F.3d 1349, 76 USPQ2d 1078 (Fed. Cir. 2005). As the *Capon* court points out, there is no requirement under written description that a specification contain a detailed description of elements where those elements are well known to those in the field:

The Board stated that "controlling precedent" required inclusion in the specification of the complete nucleotide sequence of "at least one" chimeric gene. Bd. op. at 4. The Board also objected that the claims were broader than the specific examples. Eshhar and Capon each responds by pointing to the scientific completeness and depth of their descriptive texts, as well as to their illustrative examples. The Board did not relate any of the claims, broad or narrow, to the examples, but invalidated all of the claims without analysis of their scope and the relation of claim scope to the details of the specifications.

Eshhar and Capon both argue that they have set forth an invention whose scope is fully and fairly described, for the nucleotide sequences of the DNA in chimeric combination is readily understood to contain the nucleotide sequences of the DNA components. Eshhar points to the general and specific description in his specification of known immune-related DNA segments, including the examples of their linking. Capon points similarly to his description of selecting DNA segments that are known to express immune-related proteins, and stresses the existing knowledge of these segments and their nucleotide sequences, as well as the known procedures for selecting and combining DNA segments, as cited in the specification.

Both parties argue that the Board misconstrued precedent, and that precedent does not establish a *per se* rule requiring nucleotide-by-nucleotide re-analysis when the structure of the component DNA segments is already known, or

readily determined by known procedures. The “written description” requirement implements the principle that a patent must describe the technology that is sought to be patented; the requirement serves both to satisfy the inventor’s obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. See *Enzo Biochem*, 296 F.3d at 1330 (the written description requirement “is the *quid pro quo* of the patent system; the public must receive meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time”); *Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1345-46 (Fed. Cir. 2000) (the purpose of the written description requirement “is to ensure that the scope of the right to exclude . . . does not overreach the scope of the inventor’s contribution to the field of art as described in the patent specification”); *In re Barker*, 559 F.2d 588, 592 n.4 (CCPA 1977) (the goal of the written description requirement is “to clearly convey the information that an applicant has invented the subject matter which is claimed”). The written description requirement thus satisfies the policy premises of the law, whereby the inventor’s technical/scientific advance is added to the body of knowledge, as consideration for the grant of patent exclusivity.

The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.

For the chimeric genes of the Capon and Eshhar inventions, the law must take cognizance of the scientific facts. The Board erred in refusing to consider the state of the scientific knowledge, as explained by both parties, and in declining to consider the separate scope of each of the claims. None of the cases to which the Board attributes the requirement of total DNA re-analysis, *i.e.*, *Regents v. Lilly*, *Fiers v. Revel*, *Amgen*, or *Enzo Biochem*, require a re-description of what was already known. In *Lilly*, 119 F.3d at 1567, the cDNA for human insulin had never been characterized. Similarly in *Fiers*, 984 F.2d at 1171, much of the DNA sought to be claimed was of unknown structure, whereby this court viewed the breadth of the claims as embracing a “wish” or research “plan.” In *Amgen*, 927 F.2d at 1206, the court explained that a novel gene was not adequately characterized by its biological function alone because such a description would represent a mere “wish to know the identity” of the novel material. In *Enzo Biochem*, 296 F.3d at 1326, this court reaffirmed that deposit of a physical sample may replace words when description is beyond present scientific capability. In *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003) the court explained further that the written description requirement may be satisfied “if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.” These evolving principles were applied in *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004), where the court affirmed that

the human antibody there at issue was not adequately described by the structure and function of the mouse antigen; and in *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 925-26 (Fed. Cir. 2004), where the court affirmed that the description of the COX-2 enzyme did not serve to describe unknown compounds capable of selectively inhibiting the enzyme.

The “written description” requirement must be applied in the context of the particular invention and the state of the knowledge. The Board’s rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA sequences when linked by known methods. Both parties explain that their invention is not in discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result.

The “written description” requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution. Both Eshhar and Capon explain that this invention does not concern the discovery of gene function or structure, as in Lilly. The chimeric genes here at issue are prepared from known DNA sequences of known function. The Board’s requirement that these sequences must be analyzed and reported in the specification does not add descriptive substance. The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes.

The Capon case has very recently been followed by the Federal Circuit, in *Falkner v. Inglis*, 79 USPQ2d 1001 (Fed. Cir. 2006). In a section of the opinion entitled “Recitation of Known Structure Is Not Required” the *Falkner* court, following the *Capon* decision, stated:

Indeed, a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. It would neither enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention. ... Accordingly, we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here “essential genes”), satisfaction of the written

description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences.

Id. at 1008.

The fact that tissue specific promoters were exceedingly well known as of the filing date is evidenced by evidence set forth above in the enablement section of this response.

Thus, it is submitted that there is clearly no *prima facie* basis for subject written description rejection, and that Applicants have provided evidence in support of written description. For these reasons, the Board is requested to withdraw the rejection.

C. Whether claims 1-3, 9-15, 20-21, 24, 30-32, 35-44 and 45 are properly rejected on the basis of obviousness-type double patenting of US 7,135,613.

Lastly, the Action rejects all of the pending claims (noting that the claim numbers of which are listed incorrectly) on the basis of obviousness-type double patenting (“ODP”) over US 7,135,613. The basis of the rejection is unclear from the Action. In the previous Action, mailed June 10, 2008, it is simply stated that “both sets of claims encompass a transgenic fish comprising a chimeric gene comprising a muscle specific promoter that drives the expression of a structural gene in said fish ...” Action dated 6/10/08 at page 21. Appellants note that the claims of the ‘613 patent are directed to transgenic fish *per se*.

Appellants assert that the Action fails to set forth a *prima facie* ODP rejection, that the present claims are anticipated or obvious over the specified claims of the ‘613, or *vice versa*. See MPEP §804 B.1. As noted in MPEP §804 B.1., a double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is “analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103” except that the patent principally underlying

the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103(a) rejection, the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are employed when making an obvious-type double patenting analysis. MPEP §804 B.1. clearly states that any obviousness-type double patenting rejection should make clear:

(A) The differences between the inventions defined by the conflicting claims - a claim in the patent compared to a claim in the application; and

(B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue is anticipated by, or would have been an obvious variation of, the invention defined in a claim in the patent.

Moreover, when considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992).

No such analysis has even been attempted here.

As an aside, Appellants would observe that during the prosecution of USSN 09/913,898, Applicants attempted to introduce claims consistent with the claims pending in the present application. See Applicant's Amendment dated May 9, 2003. (Exhibit 8). In response to this attempted amendment, the Examiner refused entry of the amendment: "The amendment filed on May 12, 2003 ... presenting only claims drawn to a new invention is **non-responsive** (MPEP §821.03) (underline added)," taking the position that such claims were found not to be drawn to the invention elected in that case, which later became the '613 patent. See Restriction Requirement mailed 12/18/03 and, again, the Restriction Requirement dated 7/30/03. (Exhibit 9) Thus, the PTO has already decided that the present claims are patentably distinct.

In view of the foregoing, Appellants respectfully request that the Board reverse the rejections of all claims.


Respectfully submitted,

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VIII. Claims Appendix

1. The method of claim 43, further defined as comprising the steps of:

- (a) obtaining a transgenic fish line comprising one or more chimeric genes that are positioned under the control of a promoter that drives the expression of a fluorescent protein in muscles of said fish, said promoter being a muscle specific promoter, such that said transgenic fish expresses fluorescent protein encoded by the gene in skeletal muscle at a level sufficient such that said transgenic fish fluoresces upon exposure to sunlight, wherein said transgenic fish are the offspring of an embryo line visually exhibiting expression of the fluorescent protein in essentially all muscle fibers in their trunk and further wherein transgenic founders of said line fluoresce upon exposure to sunlight; and

- (b) distributing fish of said line to the ornamental fish market.

2. The method of claim 1 or claim 43, further comprising displaying said transgenic fish under a blue or ultraviolet light.

3. The method of claim 2, wherein the transgenic fish are displayed under an ultraviolet light that emits light at a wavelength selected to be optimal for the fluorescent protein or proteins.

4. – 8. (Cancelled)

9. The method of claim 1 or claim 43, wherein the transgenic fish express a BFP.

10. The method of claim 9, wherein the transgenic fish express an EBFP.

11. The method of claim 1 or claim 43, wherein the transgenic fish express a YFP.

12. The method of claim 11, wherein the transgenic fish express an EYFP.
13. The method of claim 1 or claim 43, wherein the transgenic fish express a CFP
14. The method of claim 13, wherein the transgenic fish express an ECFP.
15. The method of claim 1 or claim 43,
wherein the transgenic fish expresses more than one color of fluorescent protein encoded
by the gene or genes.
16. – 19. (Cancelled)
20. The method of claim 1 or claim 43, wherein the promoter is a zebrafish muscle creatine
kinase gene promoter.
21. The method of claim 1 or claim 43, wherein the promoter is a zebrafish myosin light
chain 2 gene promoter.
22. – 23. (Cancelled)
24. The method of claim 1 or claim 43, wherein one or more of said chimeric genes further
comprises a ubiquitously expressing promoter.
25. – 29. (Cancelled)
30. The method of claim 15, wherein the more than one fluorescent protein is expressed in
the same tissue, to effect a new fluorescent color.
31. The method of claim 30, where the transgenic fish expresses a GFP and a BFP.

32. The method of claim 15, wherein the more than one fluorescent proteins are separately expressed in different tissues.

33. – 34. (Cancelled)

35. The method of claim 32, wherein the transgenic fish expresses a YFP under the control of a muscle specific promoter.

36. The method of claim 1 or claim 43, wherein the transgenic fish is a stable transgenic fish line obtained by a method comprising the steps of:

- (a) obtaining a transgenic fish comprising one or more fluorescence genes positioned under the control of a promoter, wherein the transgenic fish expresses one or more fluorescent proteins encoded by the one or more fluorescence genes; and

- (b) breeding the transgenic fish with a second fish to obtain offspring; and

- (c) selecting from said offspring a stable transgenic line that expresses one or more fluorescent proteins.

37. The method of claim 36, wherein the second fish is a wild type fish.

38. The method of claim 36, wherein the second fish is a second transgenic fish.

39. The method of claim 1 or claim 43, wherein the transgenic fish is a transgenic zebrafish, medaka, goldfish or carp.

40. The method of claim 36, wherein the second fish is a zebrafish, medaka, goldfish or carp.

41. The method of claim 1, 36 or 43, wherein the transgenic fish is a transgenic koi, loach, tilapia, glassfish, catfish, angel fish, discus, eel, tetra, goby, gourami, guppy, Xiphophorus, hatchet fish, Molly fish, or pangasius.

42. The method of claim 39, wherein the transgenic fish is a transgenic zebrafish.

43. A method of providing transgenic fish to the ornamental fish market, comprising the steps of:

(a) obtaining a transgenic fish line comprising one or more chimeric genes that are positioned under the control of a promoter that drives the expression of a fluorescent protein in muscles of said fish, said promoter being a muscle specific promoter, such that said transgenic fish expresses fluorescent protein encoded by the gene in skeletal muscle at a level sufficient such that said transgenic fish fluoresces upon exposure to one or more light; and

(b) distributing fish of said line to the ornamental fish market.

44. The method of claim 1 or 43, wherein the transgenic fish express a GFP.

45. The method of claim 44, wherein the transgenic fish express an EGFP.

IX. EVIDENCE APPENDIX

EXHIBIT 1. The Declaration of Zhiyuan Gong, Ph.D. (“Gong Declaration”) and its referenced exhibit (“Declaration Exhibit 1”), made of record by the Office Action Response dated October 7, 2008.

EXHIBIT 2. Moss *et al.*, made of record by the Information Disclosure Statement (Form 1449) dated November 28, 2003.

EXHIBIT 3. Higashijima *et al.*, made of record by the Information Disclosure Statement (Form 1449) dated November 28, 2003.

EXHIBIT 4. Kuo *et al.*, made of record by the Information Disclosure Statement (Form 1449) dated November 28, 2003.

EXHIBIT 5. Kim *et al.*, made of record by the Information Disclosure Statement (Form 1449) dated November 28, 2003.

EXHIBIT 6. Hackett *et al.*, made of record by the Information Disclosure Statement (Form 1449) dated November 28, 2003.

EXHIBIT 7. Gong *et al.*, made of record in the Office Action dated December 10, 2008.

EXHIBIT 8. Applicant’s Amendment, presented in the Office Action Response dated May 9, 2003.

EXHIBIT 9. Office Action and communication, mailed on December 18, 2003 (Office Action including a restriction/election requirement) and July 30, 2003 (communication further regarding the election of claims).

X. RELATED PROCEEDINGS APPENDIX

There are no other appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.